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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,486	07/31/2001	Alexander N. Glazer	B01-114-1	3672

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EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/07/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/919,486	GLAZER ET AL.
	Examiner Hope A. Robinson	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 January 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) 15, 19-24 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-14 and 16-18 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120.

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4</u> .	6) <input type="checkbox"/> Other: _____ .

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-14 and 16-18 are drawn to a recombinant cell which expresses a holo-phycobiliprotein fusion protein, classified in class 435, subclass 69.7.
 - II. Claims 19-22 are drawn to a method for making a holo-phycobiliprotein fusion protein, classified in class 435, subclass 69.1.
 - III. Claim 15 is drawn to a cell in situ, classified in class 800, subclass 4.
 - IV. Claim 23 is drawn to a recombinant cell which conditionally expresses a heterologous to the cell, fluorescent, first holo-phycobiliprotein domain, classified in class 435, subclass 70.1.
 - V. Claim 24 is drawn to a method for making a heterologous to the cell, fluorescent, first holo-phycobiliprotein domain, classified in class 435, subclass 325.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and III are patentably distinct because the cells of Invention II can be located inside a tissue or an organism.

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The products of Inventions I, III and IV are separate and distinct from the methods of Invention II and V, however, are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case the cells can be used in a materially different process such as cell culture or bioassays.

The products of Inventions I and IV are separate and distinct because the cell of Invention I is fused to another fusion partner, thus structurally different.

The methods of Inventions II and V are patentably distinct because the methods have different steps and end products.

Several of the inventions above are independent and distinct, each from the other. They have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other groups. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved.

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The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist

2. During a telephone conversation with Mr. Osman on March 26, 2003, a provisional election was made with traverse to prosecute the Invention of Group I, Claims 1-14 and 16-18. Affirmation of this election must be made by applicant in responding to this Office action. Claims 15 and 19-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142 (b), as being drawn to a non-elected invention.

Specification

3. The specification is objected to because of the following informalities:

The specification is objected to because on page 8 there appears “functionality/ies” at line 24 and line 30 for “etc., etc.”. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-14 and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and the dependent claims hereto are indefinite as the components of the fusion protein are “a first holo-phycobiliprotein domain and a heterologous protein domain” and the metes and bound as to what “heterologous protein domain” is undefined in the claim(s) and in the specification. The claim is further indefinite as to which components in the list, the cell “makes or comprises”. Claim 1 is indefinite as to “a first holo-phycobiliprotein” as this claim language implies a “second” which is not recited in the claim. Claim 1 is also indefinite as to the language “corresponding”, corresponding to what? Claim 1 appears to be incomplete as claims 2-4 recite a component needed to form the bilin recited in this claim. Note the following: *A recombinant prokaryotic or eukaryotic cell which expresses a holo-phycobiliprotein fusion protein comprising a fluorescent, heterologous to the cell first holo-phycobiliprotein domain fused to a fluorescent, heterologous to the cell second holo-phycobiliprotein domain, comprising the following components: a heme, a recombinant heme oxygenase, a bilin, a recombinant bilin reductase, a recombinant phycobiliprotein domain-bilin lyase, an apo-phycobiliprotein fusion protein precursor consisting of a apo-phycobiliprotein domain, wherein, said components react inside the cell to form the holo-phycobiliprotein fusion protein.* It is suggested that applicant

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cancel claims 2 and 3 and rewrite claim 4 to recite “*The cell of claim 1 wherein the heme oxygenase is HO1*” in view of the above proposed claim language.

Claims 5-9 are indefinite as to the recitation of “...spectroscopically distinguishable” as it is unclear how much variation (i.e. sensitivity of the equipment) is required, further, spectroscopic differences also vary based on the operator of the equipment.

Claim 13 is indefinite as the acronym (E. coli) should be spelled out and the name italicized (see also claim 14, with regard to “*in vitro*”).

in view of the above proposed claim language Claim 17 lacks antecedent basis for “the bound bilin” as independent claim does not recite that the “bilin” is bound.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

6. Claims 1-14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fairchild et al. (PNAS, vol. 89, pages 7017-7021, April 1992) taken with Allnutt et al. (U.S. Patent/PUB No. 20010055783, June 16, 2001) and Frankenberg et al. (The Plant Cell, vol. 13, pages 965-978, April 2001).

Fairchild et al. teach phycobiliproteins expressed in recombinant *Escherichia coli* cells (page 7017 and abstract). Fairchild et al. disclose proteins having the apo- α subunit and the holo- α subunit of a heterologous C-phycocyanin (abstract and page 7017). Fairchild et al. also disclose the bilin phycocyanobilin (PCB) and the protein bilin lyase CpcE and CpcF (phycocyanin α subunit phycocyanobilin lysase) see pages 7017-7018 and 7020). Fairchild et al. teach that heme is a component in the bilin biosynthesis pathway (page 7017 and abstract). Fairchild et al. does not teach a fusion protein (see pages 7017-7020). However, Allnutt et al. teach fusion proteins which have a phycobiliprotein domain and another domain corresponding to a first member of a specific binding pair, where the domain derived from the first member of the specific binding pair can be directly fused to the phycobiliprotein domain, expressed in *E. coli* (see abstract and page 6). Allnutt et al. also teach that phycobiliprotein is a fluorescent label for other proteins and as an in situ probe (page 6). Allnutt et al. further teaches that

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phycobiliprotein domains have bilin prosthetic groups (6). In-so-far-as Fairchild et al. and Allnutt et al. do not explicitly teach PcyA, Frankenberg et al. teaches this enzyme and the specific pathway (page 967). Frankenberg et al. teach that phytobilins are synthesized from heme via the intermediacy of biliverdin, the interconversion is accomplished by ferredoxin dependent heme oxygenases (page abstract and 965). Frankenberg et al. also teach that cyanobacteria and red algae possess novel ferredoxin dependent bilin reductases for the synthesis of the linear tetrapyrrole precursors such as PcyA (3Z-phycocyanobilin:ferredoxin oxidoreductase). Frankenberg et al. also teach a fusion protein (see pages 965-967).

Therefore, it would have been obvious to one of ordinary skill in the art to have had the claimed invention as a whole by combining the teachings of the above references because all three references teach phycobiliproteins (a family of proteins found in cyanobacteria, red algae etc.) and the expression of the protein in recombinant *E. coli* cells. In addition, Fairchild et al. teach the holo and apo subunits of the protein. One of ordinary skill would be motivated to combine the teachings of the references because Frankenberg et al. teach the specific pathway by which phytobilins are synthesized and the utilization of the specific enzymes recited in the claims. Moreover, although the references by Fairchild et al. and Allnutt et al. do not explicitly teach the enzymes Frankenberg demonstrates that the enzymes are a part of the pathway to obtain the end product which is taught by the all three references and claimed in the instant application. The claimed invention is within the art as Fairchild et al. teach phycobiliproteins having apo and holo subunits expressed in a recombinant cell (*E. coli*) and Allnutt et al. teach a recombinant cell

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expressing phycobiliprotein fusion protein as claimed in claim 1, and Frankenberg teaches the claimed enzymes and the pathway of the biosynthesis of bilin, indicating that the enzymes recited in claim 1 are intrinsic properties. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious

Art of Record

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tooley et al. (PNAS, vol. 98, no. 19, pages 10560-10565, September 11, 2001) teach the pathway to synthesize a fluorescent holophycobiliprotein subunit from a photosynthetic cyanobacterium.

Landgraf et al. (FEBS Letters, vol. 508, pages 459-462, 2001) teach the co-expression of two genes from the bilin biosynthetic pathway and a recombinant holophytochrome in *E. coli*.

Conclusion

8. No claims are allowable.

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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

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